REMARKS

Claims 38, 40, 41, 43, 45, 46, 49, 65-68 and 80 were pending and stand rejected under 35 U.S.C. § 101 and 112, first paragraph (written description and enablement).

Claims 43 and 80 have been canceled without prejudice or disclaimer to its reintroduction in a continuing application. Cancellation of a claim does not raise additional issues for consideration, therefore the amendments canceling these claims should be entered.

Furthermore, claims 38, 40, 45, 46, 49 and 65-80 have been amended to make explicit what was previously implicit, namely that the control element is a promoter. Amending the claims to make something explicit does not raise additional issued for consideration, therefore the amendments should be entered. Thus, claims 38, 40, 41, 43, 45, 46, 49 and 65-68 are pending as shown above.

35 U.S.C. §101

Claim 80 was rejected under 35 U.S.C. § 101 as alleged drawn to a product of nature. The cancellation of claim 80, without prejudice or disclaimer, obviates this rejection.

In addition, claims 38, 40, 41, 43, 45, 46, 49, and 65-68 were again rejected under 35 U.S.C. §101 as allegedly lacking utility. In this lengthy rejection, various grounds are set forth including the assertions that

(1) "the instant claims cover a great variety of mice that cannot be used for the asserted utility because they would not be useful in assaying agents to determine how they affect native gene expression... the claims cover a wide variety of transgenic mice that have control elements and combinations of control elements that are in no way representative of the native expression of the genes from which they are derived"

(2) a credible utility is not (and cannot be) assessed because a specific and substantial utility is lacking

(3) substantial and specific utility is not present

(4) Applicants arguments were not commensurate in scope with the claims

(5) the evidence of record, including Jankowsky et al., does not pertain to utility and

(6) Applicants are "encouraged" to amend the claims to exclude species that lack utility

(7) the specification provides no assertion of utility for artificial constructs having no bearing no "native" gene function

(8) no support is given establishing a well-established utility

Applicants again traverse the rejection and supporting remarks.

First and foremost, Applicants submit that, however misplaced the Examiner's concern regarding control elements that that do not represent native gene expression, the foregoing amendments fully address this concern by indicating that the control element is a promoter. It is abundantly plain to the skilled artisan that a promoter represents native gene expression. Accordingly, this (misplaced) basis for the rejection has been obviated.

In any event, whether the term "control element" or "promoter" is used, Applicants submit that the Office has improperly construed the claims. The specification clearly and unambiguously defines the term "control elements derived from a stress-inducible gene" to encompass only control elements that regulate transcription of at least one stress-inducible gene(s). Thus, promoters that do not regulate transcription of stress-inducible genes are not encompassed by the claims.

Interestingly, the Examiner acknowledges later in the Office Action that the claims are not so broad as to cover control elements unrelated to stress-related genes. For example, in discussing written description, it is noted that "... the prior art does not provide a description of the necessary native control elements for the very large genus of stress-inducible genes covered by the claims." (Final Office Action, page 7). Hence, it is apparent from the specification, and stated on the record herein, that only control elements that regulate transcription of a native stress-inducible gene are encompassed by the phrase "control elements derived from stress-inducible promoters."

When the claims are properly construed, it is clear that the assertions made in (1), (4) and (7) are untenable. A "great variety" of mice according to the claims that cannot be used for *in vivo* imaging do not exist inasmuch as the control elements are always related to expression of a native (stress-inducible) gene. No assertion as to utility other than studying gene expression is required because that is the substantial, credible and well-established utility.

Furthermore, in maintaining this rejection, the Examiner has taken definitions from the specification in isolation and erroneously asserted that Applicants arguments are "far afield" from what is claimed. In reality what the claimed animals comprise (a) promoters (b) derived from (c) stress-inducible genes. The definitions reproduced by the Examiner in support of the assertion that the "promoter can be any promoter at all," relate to (a) in isolation and do not take into account (b) or (c), namely that the promoter is derived from a stress-inducible gene.

When properly construed, it is clear that what is meant by a promoter derived from a stress-inducible gene is a promoter that regulates transcription of a native stress-inducible gene. Clearly, there is specific, substantial, credible and well-established utility for transgenic mice bearing such constructs.

Therefore, when properly construed, it is clear that the utility requirement has been satisfied and that Applicants arguments were commensurate in scope with the claims.

Turning to points (2) to (3), Applicants again submit that the requirements for establishing utility of the claimed subject matter have been met. The substantial and specific utility is use of the animals for analyzing biochemical pathways and physiological functions *in vivo*. *See, e.g.,* page 22 of the specification. Such uses are repeated throughout the specification as filed and clearly establish a substantial, specific and credible utility.

Furthermore, MPEP § 2107 cautions Examiners not to impose utility rejections where the assertions would be considered credible by the skilled artisan:

> If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility.

Here, the assertion that the animals are useful for studying a variety of functions *in vivo* is clearly credible to the skilled artisan (see also, U.S. Patent No. 5,650,135, cited on page 70 of the specification). The credible (along with substantial and well-established) utility is unquestionable -- *in vivo* imaging provides an extremely powerful tool for example for studying gene expression. There are no embodiments in which control elements (promoters) derived from stress-inducible genes will not be useful in studying gene expression.

Turning to point (5), the evidence of record does in fact pertain entirely to utility. This evidence includes not only Jankowsky and Dr. West's declaration, but, in addition, the teachings of the specification. Indeed, it is arguably the teachings of the specification that carry the most weight. Here, there is ample teaching regarding the use of the claimed animals for *in vivo* imaging. *See,* specification throughout and, particularly, U.S. Patent No. 5,650,135. Thus, the evidence of record does pertain to utility and establishes the rejection is improper.

With respect to (6), for the reasons noted above, when the claims are properly construed, they do not include any species that lack utility and Applicants should not be required or even encouraged to amend their claims.

Finally, the assertion made in (8) (that no support is given establishing a well established utility) is also in error. MPEP § 2107 states that:

> (3) If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

For the reasons of record and those noted above, the person of ordinary skill in the art would immediately appreciate that the claimed subject matter (which does not include animals comprising "any promoter") is useful for studying gene expression by *in vivo* imaging.

Based on the foregoing and the reasons of record, Applicants respectfully submit that the rejections under 35 U.S.C. §101, for lack of utility, should be withdrawn.

35 U.S.C. §112, First Paragraph, Written Description

Claims 38, 40, 41, 43, 45, 46, 49 and 65-68 were rejected on the grounds that Applicants' specification fails to sufficiently describe the claimed transgenic mice. (Office Action, pages 4-6).

It is well-settled law that the fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas Cath, Inc. v. Mahurkar*, 935 F.2d 1557, 19 USPQ2d 1111. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of the claimed invention at the time of filing. *Vas Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention in ipsis verba. Rather, all that is required is that the specification reasonably convey possession. See, e.g., *In re Lukach*, 169 USPQ 795, 796 (CCPA 1971).

Indeed, in the recent case of *Capon v. Eshhar* (Aug 12, 2005, Fed. Cir. 03-1480), the Federal Circuit completely rejected the notion that the specification must describe information (*e.g.*, nucleotide sequence) that is either known or can readily be determined based on scientific facts (Capon at page 15):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

Thus, any written description inquiry must begin with proper claim construction. Here, the claims on appeal are not drawn to transgenic mice comprising any and all promoters. In fact, the genus encompassed by the claims on appeal is nowhere near as broad as that painted by the Examiner -- it includes only promoters which are derived from stress-inducible genes and which drive expression of a reporter (light-generating protein).

Thus, even if the specification did not describe multiple representative species of stress-inducible promoters, conception of the claimed subject matter does not, indeed cannot, require description of every stress-inducible promoter. Satisfaction of the written description does not require a showing that the skilled artisan can predict *a priori* each and every nucleotide sequence falling within the scope of the claims, but, rather, a demonstration that one of skill in the art would be aware an applicant was in possession of methods for making animals as claimed. Here, the skilled artisan, having followed the teaching of the specification, would have no doubt that Appellant was in possession of the claimed subject matter.

Furthermore, the claimed transgenic animals must not only include multiple expression cassettes comprising stress-inducible promoters, they must have been obtained using the particularly specified method. Thus, the claims at issue are product-by-process claims and, as such, are subject to a written description test much different from that used for product claims (see, M.P.E.P. § 2163):

> ...where the process has actually been used to produce the product, the written description requirement for a product-by-process claim is clearly satisfied.

With respect to the pending claims, the product is a transgenic mouse comprising a panel of the specified expression cassettes and made using standard transgenic mouse technology. The evidence of record (including Dr. West's Declaration and Abstracts attached thereto), indicates that making such animals was standard and conventional and, therefore, described by the specification as filed.

Thus, when the pending product-by-process claims are properly construed, it is plain that they are drawn to a genus that is more than adequately described by the specification as filed.

35 U.S.C. §112, First Paragraph, Enablement

The Examiner again maintains that undue experimentation would be required in order to practice the invention of claims 38, 40, 41, 43, 45, 46, 49 and 65-68, stating that only actual production of the claimed transgenic animals would satisfy this requirement (Office Action, page 7):

> In summary, since the art of making transgenic animals is highly unpredictable and unless a transgenic mouse has been produced, one can not predict what will the characteristics of the transgenic mouse comprising a given panel of expression cassettes and therefore, an artisan would not know how to use the claimed transgenic mouse in claimed methods.

For all the reasons of record, the Examiner's rejection remains legally and factually wrong.

Making Transgenic Mice With Multiple Expression Cassettes is Predictable and Routine

Factually, there is nothing unpredictable about making transgenic mice as claimed, let alone highly unpredictable. Transgenic mice expressing light generating proteins, where light expression is driven by a promoter sequence to which the light generating protein-encoding sequences have been made repeatedly and patented, for example, as described in U.S. Patent Nos. 5,650,135; 6,217847; 6,649,143; 6,632,978; and 6,566,089.

Likewise, "predicting . . .the characteristics of the transgenic mouse" would be routine to the skilled artisan. They would instantaneously know from the specification that the claimed transgenic animals would be characterized by light-generation when administered an analyte that induces one or more of the transgenic stress-inducible control sequences. Simply put, the transgenic mice are characterized by their ability to generate light under specific conditions, and the skilled artisan would know to use them for studying regulation of stress-inducible genes, for example in response to administration of an analyte.

Thus, the allegations that (1) making transgenic mice is highly unpredictable and (2) that characteristics of such mice is unpredictable are unsustainable and completely refuted by the evidence of record.

Meeting the Enablement Requirement Does Not Require Actual Working Examples

This oft-repeated enablement rejection is also contrary to well-settled law. Legally, there is no requirement that an applicant provide working examples or actually make the claimed subject matter. See, MPEP 2164.02. Indeed, as previously noted with regard to transgenic animals, the Board of Patent Appeals and Interferences has made it abundantly clear that there can be no requirement for a disclosure of what the examiner perceives as possible characteristics of such a [transgenic animal] product. *Ex parte Chen,* 61 USPQ2d at 1028 (BPAI 2002, unpublished).

Even Patent Office Training materials recognize that claims to transgenic animals are fully enabled where "an enabled use for the claimed transgenic mouse is well established." (See, Training Materials for Examining Patent Applications with Respect to 35 U.S.C. 112, first paragraph -- Enablement, Example I, page I-6, *circa* 1997).

In the case at hand, and as noted above with the unsustainable new utility rejection, an enabled use for transgenic animals comprising expression cassettes encoding a light-generating protein is well established, as evidenced for example by U.S. Patent No. 6,217,847 which shows the generation of a transgenic animal comprising an expression cassette encoding luciferase and use of these animals for the temporal and spatial analysis of transcriptional control.

When the enablement requirement is determined relative to the pending claims, it is clear that the specification enables the skilled artisan to make and use the claimed rodents.

35 U.S.C. §102

Claim 80 was rejected under 35 U.S.C. § 102(b) as allegedly anticipated by JAX Mice Price List (1997).

The cancellation of claim 80, without prejudice or disclaimer, obviates this rejection.

CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 493-3400.

Respectfully submitted,

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